IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

IN RE:	BRENNAN, TIMOTHY J.)	
SERIAL NO:	10/033,632)	
FOR:	DRUGS FOR SPINAL ANESTHESIA)	) APPEAL NO. _____
FILED:	December 26, 2001)	
GROUP:	1616)	
EXAMINER:	GEORGE, Konata M.)	
DOCKET NO:	P05435US0)	

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs:

Please enter the following brief on appeal into the record.

I. REAL PARTIES IN INTEREST

The real party in interest is the assignee, University of Iowa Research Foundation.

The assignment is recorded on Reel 012652, Frame 0244.

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences relating to this pending application.

CERTIFICATE OF MAILING/TRANSMISSION (37 CFR 1.8(a))

I hereby certify that this correspondence is, on the date shown below, being:

MAILING

☑ deposited with the United States Postal Service with sufficient postage as First Class mail in an envelope addressed to the Commissioner for Patents, Mail Stop Appeal Brief-Patents P.O. Box 1450, Alexandria, VA 22313-1450.

Date: Nov 19, 2003

FACSIMILE

☐ transmitted by facsimile to the Patent and Trademark Office, Art Unit _____ at Fax No. (703) 872-_____.

EDMUND J. SEASE

III. STATUS OF CLAIMS

This application was originally filed with claims 1-10 including independent method claim 1 and independent composition claim 6. Claims 6-10 were cancelled during prosecution. The claims on appeal are claims 1-5, attached hereto in the Appendix. Claims 1-5 stand rejected under U.S.C. § 103(a) as being unpatentable over Arnold et al. (U.S. 5,670,516) in view of Current Therapy (1977).

IV. STATUS OF AMENDMENTS

This application was filed December 26, 2001. An amendment after final was filed August 26, 2003 and entered on 9/30/03.

V. SUMMARY OF THE INVENTION

Spinal anesthetics for intrathecal administration to produce spinal anesthesia are provided with use of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically active analogue. Specification, p. 14, lines 2-6.

Preferred compounds for use in this invention are a class of receptor antagonists/drugs, i.e. the ampa-kainate receptor antagonists. AMPA is α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) and kainate is a second subclass of these receptors. Another name for these receptors is nonNMDA ionotropic excitatory amino acid receptor antagonists (Ozawa, S., Kamiya, H. and Tsuzuki, K., Glutamate Receptors in the Mammalian Central Nervous System, Prog. Neurobiol., 54 (1998) 581-618). NMDA = N-methyl-D-aspartate. In particular, the most preferred compounds are 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or its

pharmaceutically acceptable analogues such as, for example, salt forms. These specific compounds are known but have previously been reported by this inventor as having no effect on pain after incision by local infiltration of the drug active in the incision. This is further evidence of the surprising nature of their operativeness and effectiveness as spinal anesthetics. The compounds of the present invention may be administered with conventional local anesthetic carriers such as dextrose solution (8.25 % dextrose in water, 5 % dextrose in water or 10 % dextrose in water) and saline solution (0.9 % saline). Specification, p. 3, lines 2-21.

The amount used to provide the desired spinal anesthetic effect will vary generally within the range of 0.1 mg to 3.0 mg, preferably 0.5 mg to 2.0 mg. Alternatively, the drug could be dosed by body weight. The amount used to provide the desired spinal anesthetic effect will vary generally within the range of 0.1 mg/kg to 60 mg/kg of body weight, preferably from 5 mg/kg to 40 mg/kg of body weight. Specification, p. 3, lines 22-28.

VI. ISSUE

Whether claims 1-5 are unpatentable under 35 U.S.C. § 103(a) in view of Arnold et al. (U.S. 5,670,516) and Current Therapy (1977).

VII. GROUPING OF CLAIMS

The claims should be grouped as follows:

Group 1 = claim 1

Group 2 = claim 2

Group 3 = claim 3

Group 4 = claims 4 & 5

VIII. ARGUMENT

Claims 1-5 are not obvious in view of Arnold et al. (U.S. 5,670,516) and Current Therapy (1977).

There is no prima facie case to Combine Arnold et al. with Current Therapy (1977). In order to properly combine the teachings of these references, there must be "some teaching, suggestion, or motivation . . . either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." MPEP § 2143.01 (citing In re Fine, 837 F.2d 1071 (Fed. Cir. 1988); In re Jones, 958 F.2d 347 (Fed. Cir. 1992)). Further, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP § 2143.01 (citing In re Mills, 916 F.2d 680 (Fed. Cir. 1990)). The Examiner, however, points to nothing that teaches or suggests the desirability of Applicant's combination.

In addition, it is well settled that the Patent and Trademark Office cannot pick and choose among the individual elements of assorted prior art references to recreate the claimed invention. Instead, the Patent and Trademark Office must look for some teaching or suggestion in the references to recreate the claimed invention. SmithKline

Diagnostics, Inc. v. Helena Laboratories Corp., 859 F.2d 878, 887, 8 U.S.P.Q.2d 1468, 1475 (Fed. Cir. 1988). In this instance, such teachings are lacking.

Arnold et al. teaches the use of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid as an analgesic agent and to treat spinal cord trauma. Arnold et al. does not teach the use of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid for anesthesia. Anesthesia and anesthetic are not even mentioned in Arnold et al. Current Therapy (1977) or any text or review on spinal anesthesia (Liu, S.S. and McDonald, S.B., Current Issues in Spinal Anesthesia, Anesthesiology, 94 (2001) 888-906; Stoelting, R.K. and Miller, R.D., Spinal and Epidural Anesthesia, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000d, pp. 168-184) does not mention 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or any drug of this class, the nonNMDA receptor antagonists. Nowhere in these references is there a suggestion to combine.

Analgesia is not the same as anesthesia. The following lists several reasons why it is non-obvious to produce spinal anesthesia with 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid.

Analgesia is a decrease in pain. An analgesic drug decreases a patient's report of pain. Many drugs have analgesic properties. When injected into the spinal fluid, opioids (narcotics) produce analgesia (Liu, S.S. and McDonald, S.B., Current Issues in Spinal Anesthesia, Anesthesiology, 94 (2001) 888-906; Stoelting, R.K. and Miller, R.D., Opioids, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000c, pp. 70-79). Clonidine also produces analgesia when injected into the spinal fluid around the spinal canal (Liu, S.S. and McDonald, S.B., Current Issues in Spinal Anesthesia,

Anesthesiology, 94 (2001) 888-906). These drugs by themselves do not produce spinal anesthesia (Liu, S.S. and McDonald, S.B., Current Issues in Spinal Anesthesia, Anesthesiology, 94 (2001) 888-906; Malinovsky, J.M. and Bernard, J.M., Spinal Clonidine Fails to Provide Surgical Anesthesia for Transurethral Resection of Prostate. A Dose-Finding Pilot Study, Regional Anesthesia, 21 (1996) 419-23; Stoelting, R.K. and Miller, R.D., Opioids, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000c, pp. 70-79; Stoelting, R.K. and Miller, R.D., Spinal and Epidural Anesthesia, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000d, pp. 168-184). Only drugs that have local anesthetic (sodium channel blocking) properties can produce spinal anesthesia.

Anesthesia is the complete blockade of the motor and sensory response during surgery. That is, the patient can not perceive surgery is occurring and does not respond to the surgery with any movement.

Many anesthetic drugs are not analgesics. Most analgesic drugs are not anesthetics. Narcotic analgesic drugs can not by themselves produce anesthesia (Hug, C.C., Jr., Does Opioid "Anesthesia" Exist? Anesthesiology, 73 (1990) 1-4). Nonsteroidal anti-inflammatory drugs are analgesic, but are not anesthetics (Hirota, K., Fukushi, S., Baba, S. and Matsuki, A., Flurbiprofen Does Not Change the Bispectral Index and 95% Spectral Edge Frequency During Total Intravenous Anaesthesia with Propofol and Fentanyl, European Journal of Anaesthesiology, 19 (2002) 483-6). In short, an analgesic drug is not necessarily the same as an anesthetic drug. Just because 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid is known as an analgesic does not make it obvious that it is an anesthetic. The current claims (1-5) are narrowly focused on a method of anesthesia.

Drugs producing anesthesia include volatile anesthetics which are inhaled by the patient when administered by a face mask. These volatile anesthetics are gases and are not injected into the spinal fluid. Other drugs with anesthetic properties (intravenous anesthetics) like propofol, ketamine, sodium thiopental and pentobarbitol do not produce and are not used for spinal anesthesia (Hawksworth, C. and Serpell, M., Intrathecal Anesthesia with Ketamine, Regional Anesthesia & Pain Medicine, 23 (1998) 283-8; Stoelting, R.K. and Miller, R.D., Intravenous Anesthetics, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000a, pp. 58-69; Stoelting, R.K. and Miller, R.D., Spinal and Epidural Anesthesia, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000d, pp. 168-184). Local anesthetics do produce spinal anesthesia when injected into the fluid around the spinal canal (Liu, S.S. and McDonald, S.B., Current Issues in Spinal Anesthesia, Anesthesiology, 94 (2001) 888-906; Stoelting, R.K. and Miller, R.D., Local Anesthetics, Basics of Anesthesia, Churchill Livingstone, Philadelphia, PA, 2000b, pp. 80-88). No other class of drugs, except the drugs of the current invention, when injected into the spinal fluid produce spinal anesthesia.

Therefore, it is not obvious that administration of this drug into the spinal fluid will produce spinal anesthesia. Treatment using 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid is novel because it is not a local anesthetic (specification, p. 3, lines 12-15) yet it is a spinal anesthetic. This provides the advantage of no side effect of hypotension that is associated with local anesthetics.

The Examiner states that it would have been obvious to one of ordinary skill to select intrathecal administration for the purposes of delivery of an anesthetic to the spinal cord. The underlying assumption is that 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid is known as a spinal anesthetic. There

is no teaching in Arnold et al that 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid is a spinal anesthetic. Only in applicant's disclosure is it revealed that 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid is a spinal anesthetic.

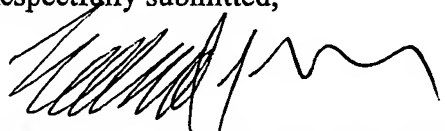
Arnold et al. reveal that 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid can treat spinal cord trauma (col. 35, line 46). However, the list of ways to administer the drug (col. 35, lines 30-34) does not include intrathecal administration. This is because treatment for spinal cord trauma is completely different than anesthesia. In patients with spinal cord trauma, drugs like this can be administered intravenously to try to reduce the damage caused by the trauma (Hugenholtz, H., Methylprednisolone for Acute Spinal Cord Injury: Not a Standard of Care, Canadian Medical Association Journal, 168(9) (2003) 1145-1146). That damage caused by nervous system trauma results in fibrosis and nerve loss. Later long-term sensory and motor dysfunction occur. Treatment of spinal cord trauma with this class of drugs attempts to prevent nerve loss secondary to injury. This is usually accomplished by injecting a drug into a vein immediately after trauma has occurred. Id. For spinal anesthesia, the intrathecal injection delivers the drug to the fluid surrounding the spinal cord. The method and purpose for using 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid are distinct between Arnold et al. and the present invention.

VIIII. CONCLUSION

For the above-stated reasons, it is submitted that the claims are in a condition for allowability. The decision of the Examiner, therefore, should be reversed and the case allowed.

Enclosed herein please find the appeal brief in triplicate and required fee of $330. If this amount is not correct, please consider this a request to debit or credit Deposit Account No. 26-0084 accordingly.

Respectfully submitted,



EDMUND J. SEASE, Reg. No. 24,741
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No: (515) 288-3667
Fax No: (515) 288-1338
CUSTOMER NO: 22885

Attorneys of Record

- pw -

APPENDIX

Claim 1 (Previously presented): A method of inducing spinal anesthesia, comprising: administering spinally a small but anesthesia producing amount of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically active analogue hereof to a patient in need of a spinal anesthetic.

Claim 2 (Original): The method of claim 1 wherein the administering spinally is by intrathecal administration.

Claim 3 (Previously presented): The method of claim 2 wherein 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically active analogue is administered in conjunction with a pharmaceutically acceptable carrier for 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or its biologically active analogue.

Claim 4 (Previously presented): The method of claim 2 wherein the dose of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically active analogue administered is from 0.1 mg to 3.0 mg.

Claim 5 (Previously presented): The method of claim 2 wherein the dose of 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically active analogue administered is from 0.5 mg to 2.0 mg.

Claims 6-10 (Canceled).